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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/880,748	06/15/2001	Steven M. Ruben	PF523P1	5654

22195 7590 09/28/2005

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EXAMINER	
DUFFY, PATRICIA ANN	
ART UNIT	**PAPER NUMBER**
1645	

DATE MAILED: 09/28/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 09/880,748	**Applicant(s)** RUBEN ET AL.	
	Examiner Patricia A. Duffy	**Art Unit** 1645	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 04 August 2005 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: _____.
   Claim(s) rejected: *97-100,119-127 and 130-152*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☒ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☒ Other: 892.

Patricia A. Duffy
Primary Examiner
Art Unit: 1645

Continuation of 11. does NOT place the application in condition for allowance because: The amendment to the specification has been entered. The objection to the specification and rejection of the claims is maintained in part as drawn to the corrections involving the inclusion of the last serine in the linker as the first amino acid in the V region. As previously set forth, the response and sequence comparision indicates the linker in the single chain antibody generated by recombinant means has the specific structure of (Gly 4Ser)3. Conventional Kabat and Wu counting back from the invariant cystine to identify the first amino acid in the V region would indicate that there is a missing amino acid. Therefore, the skilled artisan would recognize that there is an error. However, the skilled artisan would not recognize that the error correction would be "serine" because of the specific structure of the linker used indicates that the last serine is part of the linker and not the V region and the skilled artisan cannot come to any conclusion regarding the identity of the missing amino acid because of the lack written description in the specification as filed with regard to the specifics of the recombinant cloning methodology employed. Further, the specification indicates that the origin of the cloned regions may be human and the skilled artisan in the antibody art recognizes that there are many different groups of human light chains, all which may start with amino acids that are not serine as evidenced by Kabat et al Sequences of Proteins of Immunological Interest Forth Edition, 1987. Kabat et al teach that in human kappa light chains, there are at least 5 different amion acids that frame the beginning of the framework region and included Asp, Val, Ala, Glu and Lys but not Ser. Kabat et al teach that in human lambda light chains, there are at least 5 different amion acids that frame the beginning of the first framework region of the variable domain and include Gln, Phe, Tyr, Asp and Ser. Therefore, although one skilled in the art would recognize that there was a missing amino acid at the beginning of the framework region by counting back from the invariant cysteine, the correction is not readily apparent because the lambda light chains of the art can alternatively begin with aminio acids Gln, Phe, Tyr, Asp or Ser and that the specific linker used to form the recombinant antibody encomasses the serine for which applicants have amended the light chain to include and thereby modifying the length of the linker which is in direct contrast to the teaching of the specification that identifies a specific structure for the linker of the recombinant antibody. There is no evidence of record that establishes that the cloning methodology as described in the specification resulted in the dropping of the serine from the end of the variable region of the cloned antibody or mutated from "Q", the closest match. A correction of an obvious error requires a two-pronged test . 1st the error must be obvious and second the correction must be obvious. Again, while one skilled in the art would recognize that there is an error in the delineation of the V region, the solution is not similarly obvious to the skilled artisan because of the variety of amino acids known to be at position 1 in sequenced human light chains. Similar differences are observed for sequenced murine V regions.

All objections and rejections are maintained.